REMARKS

Applicants respectfully request reconsideration of the pending claims in view of the above amendments and the following remarks.

Applicants thank Examiner for rejoining the claims of Groups I-IV. Claims 30, 38, 50, 56, 60, 64-71, 77-80, 84, and 86-101 have been canceled without prejudice or disclaimer. Claims 31-37, 39-47, 51-55, 57-59, 61-63, 72-74, 81-83, and 85 have been amended. Claims 31-37, 39-49, 51-55, 57-59, 61-63, 72-76, 81-83, and 85 are currently pending.

No new matter has been inserted. Claim 31 was amended to include the features of claim 30 and to include SEQ ID NO's. Claims 32-37, 40-44, 52-55, 58-59, 62, and 82 were amended to include SEQ ID NO's. Claims 39, 57, 61, 81, 83, and 85 were amended to change their dependence and include SEQ ID NO's. Claims 45, 63, and 72 were amended to change their dependence. Claims 46 and 47 were amended to include the features of claim 31. Claim 51 was amended to include the features of claim 50 and to include SEQ ID NO's. Claims 73 and 74 were amended to include the features of claim 51.

35 U.S.C. § 112, written description

Claims 30-47, 50-74, 77-88, and 91-99 were rejected under 35 U.S.C. § 112, first paragraph, for written description. Applicants respectfully traverse this rejection.

Specifically, the Examiner states that since no baseline sequence is provided for the "wild-type" SPE-A, none of the mutant proteins claimed meet the written description requirement. However, as amended, claims 31-37, 39-44, 46-47, 51-55, 57-59, 61-62, 73-74, 81-83, and 85 now include SEQ ID NO's of a wild type sequence and therefore Applicants assert that the written description requirement has been met.

To the extent that the Examiner maintains this rejection, the Applicants point out that according to MPEP § 2163 "there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed" (emphasis added). See *In re*

Wertheim, 541 F.2d 257, 263 (C.C.P.A. 1976). Possession may be shown in a variety of ways including through description of an actual reduction to practice and describing distinguishing identifying characteristics sufficient to shown that the applicant was in possession of the claimed invention. See MPEP § 2163; *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68 (1998).

In this case, Applicants have provided both descriptions of actual reduction to practice and distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. The examples describe 9 SPE-A mutants that were made and evaluated. Four of the nine were tested for lethality, and two were determined to be nonlethal. Further, the specification specifically discloses 5 secondary structural features of this relatively small protein (220 amino acids) that are suitable locations for mutations yielding a nonlethal protein along with a functional explanation for the importance of these structural features. Therefore, the specification clearly conveys the information that the Applicant has invented the subject matter which is claimed and consequently the written description requirement has been satisfied.

35 U.S.C. § 112, enablement

Claims 30-45, 50-72, 77-86, and 91-97 were rejected under 35 U.S.C. § 112, first paragraph, for enablement. Applicants respectfully traverse this rejection.

Specifically, the Examiner states that since no baseline sequence is provided for the "wild-type" SPE-A, one of skill in the art would not be able to make and use the claimed SPE-A mutants. However, claims 30 and 50 have been canceled and, as amended, claims 31-37, 39-44, 46-47, 51-55, 57-59, 61-62, 73-74, 81-83, and 85 now include SEQ ID NO's of a wild type sequence. Therefore, Applicants assert that the enablement requirement has been met. Applicants respectfully request that this rejection be withdrawn.

To the extent the Examiner maintains this rejection, Applicants point out that the MPEP, at § 2164.08, indicates that "the scope of enablement must only bear a 'reasonable correlation' to

the scope of the claims." In this case, the claims relate to a mutant SPE-A toxin comprising from one to six specific mutated residues from a recited sequence. Further, the Applicants have provided a disclosure that is broadly enabling. The specification specifically discloses 5 secondary structural features of this relatively small protein (220 amino acids) that are suitable locations for mutations yielding a nonlethal protein. This extensive description of suitable regions of the protein is disclosure commensurate with the scope of claims drawn to one to six specific mutated residues. Thus, the present disclosure meets the standard for enablement as described in the MPEP at § 2164.08.

The MPEP notes that an enabling disclosure can include either specific examples or broad terminology. The present application includes working examples demonstrating the production of specific nonlethal SPE-A mutants, provides specific description of 5 secondary structural features that are suitable sites for mutations, and explicitly calls out 41 amino acids preferred as residues to be mutated, of which 6 residues are featured in the claims. Therefore, the present disclosure meets the standard for enablement as described in the MPEP at 2164.08 and in re Marzocchi.

Not only does the present application specifically identify particular regions and residues of SPE-A that are suitable for mutation, it provides working examples detailing success in producing several nonlethal SPE-A mutants. The examples describe 9 SPE-A mutants that were made and evaluated. Four of the nine were tested for lethality, and two were determined to be nonlethal. For at least these reasons, Applicants respectfully request that this rejection be withdrawn.

Claims 46, 48, 73, 75, 87, 89, 98, and 100 were separately rejected under 35 U.S.C. § 112, first paragraph, for enablement. Applicants respectfully traverse this rejection.

The Examiner concedes that the specification is enabling for SPE-A vaccines designated SPE-A N20D, D45N, N20D/C98S, N20D/K157E, and N20D/D45N/C98S. However, the Examiner asserts that claims encompassing other mutants are not enabled, in part, because

Applicants have not included a SEQ ID NO in the claims. In response, the Applicants have canceled claims 30 and 50 and have amended claims 31-37, 39-44, 46-47, 51-55, 57-59, 61-62, 73-74, 81-83, and 85 to include SEQ ID NO's. Applicants respectfully request that this rejection be withdrawn.

To the extent that the Examiner maintains this rejection, Applicants again point out that the MPEP, at § 2164.08, indicates that "the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims." As the Applicants have provided numerous working examples in additional to structural information regarding suitable mutants, the standard for enablement has been met and Applicants respectfully request that this rejection be withdrawn.

Claims 47, 49, 74, 76, 88, 90, 99, and 101 were separately rejected under 35 U.S.C. § 112, first paragraph, for enablement. Applicants respectfully traverse this rejection.

The Examiner concedes that the specification is enabling for pharmaceutical compositions comprising mutant SPE-A proteins designated SPE-A N20D, D45N, N20D/C98S, N20D/K157E, and N20D/D45N//C98S. However, the Examiner asserts that claims encompassing compositions comprising other mutants are not enabled, in part, because Applicants have not included a SEQ ID NO in the claims. In response, the Applicants have canceled claims 30 and 50 and have amended claims 31-37, 39-44, 46-47, 51-55, 57-59, 61-62, 73-74, 81-83, and 85 to include SEQ ID NO's. Applicants respectfully request that this rejection be withdrawn.

To the extent that the Examiner maintains this rejection, Applicants again point out that the MPEP, at § 2164.08, indicates that "the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims." As the Applicants have provided numerous working examples in additional to structural information regarding suitable mutants, the standard for enablement has been met and Applicants respectfully request that this rejection be withdrawn.

35 U.S.C. § 102

Claims 30-47, 50-74, 77-88 and 91-99 were rejected under 35 U.S.C. 102(b) as anticipated by Weeks et al. (Infect. Immun., 52(1):144-150 (1986)). Applicants respectfully traverse this rejection.

Examiner asserts that since Applicants did not include a sequence in the claim language that the claimed SPE-A mutants are anticipated by all SPE-A species. While not conceding the correctness of Examiner's position, in the interest of advancing prosecution, Applicants have canceled claims 30 and 50 and amended claims 31-37, 39-44, 46-47, 51-55, 57-59, 61-62, 73-74, 81-83, and 85 to include SEQ ID NO's in order to obviate this rejection. Therefore, as Weeks does not disclose any of the mutated residues required by the current claims, it is clear that claims 30-47, 50-74, 77-88 and 91-99 are not anticipated by Weeks et al. Applicants respectfully request that this rejection be withdrawn.

Claims 30-47, 50-74, 77-88 and 91-99 were rejected under 35 U.S.C. 102(b) as anticipated by Johnson et al. (Mol. Gen. Genetics, 203:354-356 (1986)). Applicants respectfully traverse this rejection.

Examiner asserts that since Applicants did not include a sequence in the claim language that the claimed SPE-A mutants are anticipated by all SPE-A species. While not conceding the correctness of Examiner's position, in the interest of advancing prosecution, Applicants have canceled claims 30 and 50 and amended claims 31-37, 39-44, 46-47, 51-55, 57-59, 61-62, 73-74, 81-83, and 85 to include SEQ ID NO's in order to obviate this rejection. Therefore, as Johnson does not disclose any of the mutated residues required by the current claims, it is clear that claims 30-47, 50-74, 77-88 and 91-99 are not anticipated by Johnson et al. Applicants respectfully request that this rejection be withdrawn.

Summary

In summary, each of claims 31-37, 39-49, 51-55, 57-59, 61-63, 72-76, 81-83, and 85 are in condition for allowance and notification to that effect is solicited. The Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below, if the Examiner believes that doing so will expedite prosecution of this patent application.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903
(612) 332-5300

Date: Jan 27, 2003

Mark T. Skoog
Reg. No. 40,178
MTS:MED:kf

23552
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